

59/485879

93

416 Rec'd PCT/PTO 16 FEB 2000

PCT/EP98/05360

P A T E N T   C L A I M S

1. Method for the multiple characterization of disseminated and micrometastasized cancer cells on the basis of DNA and/or RNA, wherein cells obtained from body fluid from an individual are investigated for at least one cancer-specific gene on the basis of mRNA; and  
cancer cells removed from body fluid from an individual are investigated for at least one cancer-specific gene on the basis of DNA and/or mRNA.
2. Method according to Claim 1, characterized in that expression analyses on the basis of mRNA are carried out on those cancer-specific genes which are essentially not expressed in non-cancer cells in the body fluid investigated.
3. Method according to Claim 2, characterized in that mRNA of the CEA, CK20, MUC1, tyrosinase and/or MAGE3 genes is investigated.
4. Method according to Claim 1, characterized in that genomic DNA of the p53, erb-B2, c-myc, K-ras, RB, APC and/or DCC genes is investigated.
5. Method according to any of the preceding claims, characterized in that genomic DNA is investigated for mutations, amplifications, LOHs, translocations and/or polymorphisms of oncogenes and/or mutated tumour suppressor genes.
6. Method according to any of the preceding claims, characterized in that the cells and/or the cancer cells are additionally investigated for at least one cancer-associated gene.

7. Method according to Claim 6, characterized in that investigation is for tissue-specific genes, metastasis-associated genes, steroid hormone receptor genes, drug resistance genes and/or genes which correlate with immunomodulation, cell proliferation and/or apoptosis.
8. Method according to Claim 7, characterized in that investigation is for metastasis-associated genes which code for angiogenesis factors, motility factors, growth factors, matrix degradation factors such as proteinases and their inhibitors, and/or adhesion factors such as adherins.
9. Method according to any of Claims 6 to 8, characterized in that mRNA is investigated.
10. Method according to Claim 9, characterized in that mRNA of the bFGF, bFGF-R, VEGF, VEGF-R1, VEGF-R2, MMP2 and/or TIMP3 genes is investigated.
11. Method according to any of the preceding claims, characterized in that cancer cells are removed from the body fluid or from cell-containing fractions thereof by immunoabsorption, microfiltration or density gradient centrifugation.
12. Method according to Claim 11, characterized in that single cancer cells are removed and are also investigated singly.
13. Method according to any of the preceding claims, characterized in that an investigation established with cancer cells is also carried out with non-cancer cells from the same individual for comparison.
14. Use of the method according to any of Claims 1 to 13 for the in vitro diagnosis of cancer.

15. Use of disseminated and micrometastasized cancer cells characterized by the method according to any of Claims 1 to 13 for testing active substances for an antineoplastic effect.
16. Means for carrying out the method according to any of Claims 1 to 13, comprising suitable primers, probes and/or positive/negative controls and, where appropriate, other means usual for the characterization of DNA and/or RNA.
17. Means according to Claim 16 in the form of a combination of test kits and/or diagnostic kits.

*Add C6*